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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

## PRELIMINARY AMENDMENT

On page 1, line 2, after the title, insert:

APPLICANTS: Wands et al.

FILED: Herewith

This application is a divisional of patent application U.S. Serial Number 09/436,184, filed on November 8, 1999, the entire contents of which is hereby incorporated by reference.

11/09/00 11:09 AM 11/09/00 11:09 AM

APPLICANTS: Wands et al.

FILED: Herewith

In the claims:

Cancel claims 1-22 and 26-38.

Add new claims 39-53.

APPLICANTS: Wands et al.

FILED: Herewith

39. The method of claim 23, wherein said compound is a vitamin D analogue.
40. The method of claim 23, wherein said compound is EB1089.
41. The method of claim 23, wherein said compound is Wortmannin.
42. The method of claim 23, wherein said compound blocks and IRS phosphorylation site of  
SEQ ID NO:5.
43. The method of claim 23, wherein said compound binds to residues 46, 465, 551, 612,  
632, 662, 732, 941, 989, or 1012 of SEQ ID NO:5.
44. The method of claim 23, wherein said tumor is selected from the group consisting of  
colon cancer, breast cancer, pancreatic cancer, liver cancer, and cancer of the bile ducts.
45. The method of claim 23, wherein said tumor is a cancer of the central nervous system.
46. The method of claim 23, wherein said tumor is a hepatocellular carcinoma.
47. The method of claim 23, wherein said tumor is a cholangiocarcinoma.
48. The method of claim 23, wherein said compound is an antibody or fragment thereof.
49. The method of claim 23, wherein said compound is a dominant negative IRS mutant.
50. The method of claim 49, wherein said mutant comprises a mutation at position 897 of  
SEQ ID NO:5.
51. The method of claim 49, wherein said mutant comprises a mutation at position 1180 of  
SEQ ID NO:5.
52. The method of claim 23, wherein said tumor is a glioblastoma.
53. The method of claim 23, wherein said tumor is a neuroblastoma.

APPLICANTS: Wands et al.

FILED: Herewith

## REMARKS

Claims 23-25, and 39-53 are pending, claims 1-22 and 26-38 having been canceled as being drawn to a non-elected invention. New claims 39-53 have been added. New claims 39-43 are supported by disclosure on page 8, lines 5-21, of the specification. New claims 44-45 are supported by disclosure on page 1, lines 25-31, of the specification. New claims 46-47 are supported by disclosure on page 22, lines 5-6, of the specification. New claim 48 is supported by disclosure on page 52, lines 11-14, of the specification. New claims 49-51 are supported by disclosure on page 48, line 28, to page 49, line 17, of the specification. New claims 52-53 are supported by disclosure on page 17, line 29, and on page 41, lines 30-33, of the specification.

No new matter has been added by this amendment.

## CONCLUSION

Applicants believe that the claims are in condition for allowance. The Commissioner is authorized to credit any overpayment or charge any deficiencies to Deposit Account No. 50-0311, Reference No. 21486-032.

Respectfully submitted,

  
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Attorney for Applicants  
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Boston, Massachusetts 02111  
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Fax: (617) 542-2241

APPLICANTS: Wands et al.

FILED: Herewith

### Appendix

#### In the specification:

On page 1, line 2, after the title, insert:

--This application is a divisional of patent application U.S. Serial Number 09/436,184, filed on November 8, 1999, the entire contents of which is hereby incorporated by reference.--

#### In the claims:

Cancel claims 1-22 and 26-38.

Add claims 39-53.

--39. The method of claim 23, wherein said compound is a vitamin D analogue.--

--40. The method of claim 23, wherein said compound is EB1089.--

--41. The method of claim 23, wherein said compound is Wortmannin.--

--42. The method of claim 23, wherein said compound blocks and IRS phosphorylation site of SEQ ID NO:5.--

--43. The method of claim 23, wherein said compound binds to residues 46, 465, 551, 612, 632, 662, 732, 941, 989, or 1012 of SEQ ID NO:5.--

--44. The method of claim 23, wherein said tumor is selected from the group consisting of colon cancer, breast cancer, pancreatic cancer, liver cancer, and cancer of the bile ducts.--

--45. The method of claim 23, wherein said tumor is a cancer of the central nervous system.--

APPLICANTS: Wands et al.

FILED: Herewith

- 46. The method of claim 23, wherein said tumor is a hepatocellular carcinoma.--
- 47. The method of claim 23, wherein said tumor is a cholangiocarcinoma.--
- 48. The method of claim 23, wherein said compound is an antibody or fragment thereof.--
- 49. The method of claim 23, wherein said compound is a dominant negative IRS mutant.--
- 50. The method of claim 49, wherein said mutant comprises a mutation at position 897 of SEQ ID NO:5.--
- 51. The method of claim 49, wherein said mutant comprises a mutation at position 1180 of SEQ ID NO:5.--
- 52. The method of claim 23, wherein said tumor is a glioblastoma.--
- 53. The method of claim 23, wherein said tumor is a neuroblastoma--

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